Perfluorocarbon NVX-428 reduced secondary brain injury in a Swine Model of Traumatic Brain Injury

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BACKGROUND

• An early intervention to mitigate secondary traumatic brain injury hypoxia may be beneficial to preserve neurological functions and prevent further damage.

HYPOTHESIS

• Administration of the perfluorocarbon emulsion NVX-428 (NuvOx Pharma LLC, Tucson, AZ) after TBI could mitigate neurological damage caused by hypoxia in a Fluid Percussion Traumatic Brain Injury (FP-TBI) swine model.

MATERIALS

• Dodecafluoropentane (DDFP), carries 200x more oxygen/gram than previously second generation perfluorocarbons which may be advantageous in treating patients with TBI.

Fig 1: DDFP emulsion NVX-428:

• 2% weight/volume.
• 250-350 nm in diameter.
• Terminal half-life 90 minutes.
• Clears via exhalation.

METHODS

• Anesthetized Yorkshire swine received FP-TBI at Time 0 (T0), followed by a bolus of NVX-428 (1ml/kg) at T15 (TBI-NVX) or no treatment (TBI-NON) and euthanized after 6 hour observation.
• Brains were fixed 10% buffered formalin solution for 48 and coronal slices were mounted and stained using hematoxylin and eosin (H&E) and Fluoro-Jade B for light and fluorescent microscope examination.
• Injury score was rated for hemorrhage, spongiosis, inflammation, edema and ischemic neurons by a veterinary pathologist who was blinded to the groups.
• Data was analyzed using independent sample T-Test. P-values < 0.05 were considered statistically significant.

RESULTS

TBI-NVX animals had lower scores for spongiosis, ischemic neurons, hemorrhage, edema and rarefaction. However, this did not reach statistical significance (p=0.165).

In the cerebellum, spongiosis was significantly less severe in TBI-NVX (mean score 1.6 ± 0.3) than in TBI-NON (mean score of 3.0±0.4) animals. Also, TBI-NVX (mean score of 2.4±0.4) was significantly lower than TBI-NON (mean score of 3.7±0.4) in ischemic neurons.

CONCLUSION

• In this swine model of TBI, administration of the perfluorocarbon NVX-428 resulted in lower injury scores for spongiosis and ischemic neurons in the cerebellum as well as a decreased number of Fluoro-Jade B positive purkinje cells.
• This data suggests that NVX-428 may play a role in mitigating secondary brain damage.
• Further studies are indicated to elucidate the potential benefits of NVX-428.